REMARKS

Claims 1-13, 15, 38 and 39 are currently pending in the application. New claim 40 has been added. Claims 1-7, 10, and 39 have been amended to address the Examiner's enablement, written description, and indefiniteness rejections. Support for these amendments can be found, e.g., at paragraphs [0048], [0075], [0158] and Table 1A. Consequently, no new matter has been added by the way of these amendments. Consideration of the amendments and remarks presented herein is respectfully requested.

I. Claim Objections

Claim 39 has been objected to for allegedly containing nonelected subject matter. The Examiner argues that the SEQ ID NOs mentioned in the claim constitute nonelected subject matter. (*Office Action*, at page 2). Applicants respectfully disagree.

In the Response to Restriction Requirement, dated September 6, 2006, Applicants elected to prosecute claims directed to an antibody that binds IL-21R. Upon this election, Applicants were also required to elect one species. In the interview with the Examiner conducted July 24, 2006, the Examiner clarified that Applicants were required to elect one antibody and the corresponding sequences, as indicated in Table 1A of the specification. Thus, Applicants elected to prosecute claims to the 18A5 antibody, and corresponding sequences, i.e., SEQ ID NOs:65-73 (representing amino acid sequences related to 18A5 antibody) and SEQ ID NOs:74-82 (representing nucleic acid sequences related to 18A5 antibody). Since claim 39 is directed to an antibody comprising SEQ ID NOs:68, 69, 70, 71, 72, or 73 (i.e., CDR sequences of 18A5 antibody), Applicants submit that the SEQ ID NOs recited in claim 39 do not constitute

nonelected subject matter. Thus, Applicants respectfully request the withdrawal of the objection to claim 39.

In addition, Applicants preemptively note that the SEQ ID NOs mentioned in new claim 40 (i.e., SEQ ID NO:65, representing the V_H domain of the 18A5 antibody, and SEQ ID NO:66, representing the V_L domain of the 18A5 antibody) also represent elected antibody species; and, therefore, do not constitute nonelected subject matter.

II. Written Description Rejection

(a) Written Description of IL-21R

The Examiner maintains the rejection of claims 1-13, 15, 38 and 39 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner argues that the genus of a polypeptide with at least 85% identity to either human or mouse IL-21R, or a fragment thereof, wherein said polypeptide is capable of binding IL-21, is not adequately described in the specification as to convey to one skilled in the art that Applicants had possession of the claimed invention. (*Office Action*, at pages 2-5). The Examiner argues that the remaining 15% of the IL-21R is not described until reduction to practice, and that the breadth of the claims is such that the evidence previously presented by Applicants to support written description is insufficient. (*Id.*, at page 3). The Examiner contends that the correspondence between antigenic epitopes of IL-21R and the undisclosed portion of 15% of the antigen polypeptide is not clear. (*Id.*, at page 4). However, the Examiner suggests that the specification provides adequate description for murine and human IL-21R sequences, as well as for antibodies that bind to specific epitopes within the 85% of the genus claimed. (*Id.*, at pages 5 and 3, respectively).

Applicants have amended the claims to recite that the antibodies must bind to an extracellular domain of a human or a mouse IL-21R. Applicants submit that the extracellular regions of IL-21Rs to which the claimed antibodies must bind are adequately described in the specification, and one skilled in the art would recognize that Applicants were in possession of such antibodies and antigens. For example, the specification provides sequences of human and mouse IL-21R polypeptides, i.e., SEQ ID NO:43 and SEQ ID NO:45, respectively. (*Specification*, at paragraph [0048]). In addition, the specification discloses that the 18A5 antibody was isolated by selection on an IL-21R-expressing cell line, hBaf3Mu-1. Thus, the 18A5 antibody must logically bind to an epitope on the extracellular domain of IL-21R. (*Id.*, at paragraph [0158]). The specification also discloses that the amino acid sequence of the extracellular domain of human IL-21R is represented by amino acids 20-235 of SEQ ID NO:43, and that the amino acid sequence of the extracellular domain of mouse IL-21R is represented by amino acids 20-236 of SEQ ID NO:45. (*Id.*, at paragraph [0075]). In addition, one skilled in the art would know that the extracellular domain of IL-21R is the domain of the protein responsible for ligand binding. Thus, Applicants respectfully submit that they have provided an adequate written description of the polypeptides that the claimed antibodies bind by describing several species, providing exemplary sequences and structures, and providing antigen functionality. Therefore, Applicants have also adequately described the claimed antibodies. For at least these reasons, Applicants respectfully request withdrawal of this written description-based rejection of the pending claims.

(b) Written Description of the Antibody

The Examiner argues that, in some instances, the antibody subjects of claims (presumably claims 4 and 5) are not allegedly adequately described. The Examiner agrees that three CDRs can be sufficient for antibody functionality, but since the previously presented claims recited antibodies with less than three CDRs, the Examiner asserts that such antibodies lack an adequate written description.

Applicants have amended claim 4 to recite an antibody comprising the CDR sequences set forth in SEQ ID NOs:68, 69 and 70, or conservative substitutions thereof, and claim 5 to recite an antibody comprising the CDR sequences set forth in SEQ ID NOs:71, 72 and 73, or conservative substitutions thereof. Thus, Applicants respectfully submit that the antibodies that are now the subject of claims 4 and 5 comprise at least three CDR sequences, and therefore are adequately described. For at least these reasons, Applicants respectfully request withdrawal of this written description-based rejection of the claims.

III. Enablement Rejection

The Examiner has also rejected claims 1-13, 15, 38 and 39 under 35 U.S.C. § 112, first paragraph, as allegedly nonenabled. The Examiner argues that because the claims recite an antibody to a polypeptide with at least 85% identity to the polypeptide set forth in SEQ ID NO:43 or SEQ ID NO:45, 15% of the protein is not adequately described; thus, one skilled in the art would not have known how to make antibodies to the undisclosed protein. (*Office Action*, at page 6). However, the Examiner states that the specification is enabling for antibodies that bind the murine or the human IL-21R of SEQ ID NOs:43 or 45, or a sequence at least 95% identical to these SEQ ID NOs. (*Id.*)

Applicants have amended the claims to recite antibodies that bind an extracellular domain of a human or a mouse IL-21R. As human and mouse IL-21Rs are enabled, Applicants respectfully submit that they have enabled antibodies that bind to an extracellular domain of such IL-21Rs. For at least these reasons, Applicants respectfully submit that the enablement rejection of claims 1-13, 15, 38 and 39 has been overcome, and respectfully request withdrawal of this enablement-based rejection.

IV. Indefiniteness Rejection

The Examiner maintains the rejection of claims 1-13, 15, 38 and 39 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. Applicants have amended the claims to recite an antibody that binds to an extracellular domain of a human or mouse IL-21R. Applicants submit that the Examiner's rejection is now overcome, and respectfully request withdrawal of this indefiniteness-based rejection of the claims.

Applicants also note that the Examiner argues that claims 4 and 5 contain language that does not properly describe the antibodies. (*Office Action*, at page 7) . Applicants understand this as the maintenance of the indefiniteness rejection of claims 4 and 5 because the phrase "conservative substitutions thereof" is allegedly indefinite. (See *Office Action,* dated November 28, 2006). Applicants respectfully traverse this rejection.

MPEP § 2173 states that in reviewing claims for compliance with 35 U.S.C. § 112, second paragraph, the Examiner must consider the claim as a whole to determine whether it apprises one of ordinary skill in the art of its scope, and therefore, serves the notice function required by 35 U.S.C. § 112, second paragraph, by providing clear warning to others as to what constitutes infringement of a claim. Definiteness of claim language must be analyzed in light of:

(A) the content of the application disclosure; (B) the teachings of the prior art; and (C) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. (*Id.*). If the language of the claim is such that a person of ordinary skill in the art could interpret the metes and bounds of the claim so as to understand how to avoid infringement, then an indefiniteness rejection is not appropriate. (See *Morton Int'l Inc. v. Cardinal Chem. Co.*, 5 F.3d 1454, 1470 (Fed. Cir. 1993)).

Applicants respectfully submit that the claim language, when read in light of the content of the application disclosure and with the interpretation that would be given by one possessing the ordinary level of skill in the pertinent art, provides sufficient notice regarding what would constitute infringement of the pending claims. The claims, as presently amended, refer to antibodies comprising the recited CDRs or conservative substitutions thereof. As Applicants argued in the Amendment dated March 27, 2007, the specification describes the term "conservative amino acid substitution" as a substitution of a native amino acid with a nonnative amino acid "such that there is little or no effect on the polarity or charge of the amino acid residue at that position." (*Specification*, at paragraph [0082]). In addition, the specification teaches that "[c]onservative modifications will produce molecules having functional and chemical characteristics similar to those of the molecule from which such modifications are made." (*Id.*, at paragraph [0081]). Thus, one skilled in the art would understand that the claims encompass antibodies having functional and chemical characteristics similar to those of antibodies comprising the recited CDRs, and that producing an antibody with mere conservative amino acid substitutions in the disclosed sequences would constitute infringement of the pending claims.

For at least these reasons, Applicants respectfully request withdrawal of this indefiniteness-based rejection of claims 4 and 5.

V. Rejection based on 35 U.S.C. § 102(b)

The Examiner has rejected claims 6-13, 15, 38 and 39 under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over WO200069880 ("Hodge"). In the Office Action dated November 28, 2006, the Examiner rejected claims 4, 5, 8-13, 15, and 38, alleging that "the antibody of Hodge would have contained at least a number of the CDR regions enumerated in the instant application." (*Office Action*, dated November 28, 2006, at page 9). Applicants acknowledge the apparent withdrawal of the obviousness rejection of claims 4 and 5 over Hodge. In the present Office Action, the Examiner argues that because Applicants do not claim specific antibodies but rather antibodies that compete with the antibodies of the invention, "the antibodies of Hodges are more likely than not able to compete with the antibodies claimed in the instant Application." (*Office Action,* at page 8, emphasis added). For the following reasons, that rejection is respectfully traversed.

To establish anticipation by inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." (MPEP § 2112, citing *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999), emphasis added). In relying upon the theory of inherency, an examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of

the applied prior art. (*Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. Inter. 1990, emphasis in the original)). Thus, in order to establish inherency, the Examiner must provide a basis in fact and/or technical reasoning to demonstrate that Hodge necessarily provides antibodies that compete for the same epitope on the IL-21R as the 18A5 antibody of the present invention. However, the Examiner has used an inappropriate standard, i.e., "more likely than not," in order to attempt to establish anticipation by inherency.

Hodge claims an antibody that selectively binds to the human IL-21R. However, Hodge does not claim or disclose any particular antibody sequence, less so the specific antibodies of the present invention, e.g., 18A5. "A prior art reference that discloses a genus does not inherently disclose all species within that broad category." (See *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings,* 370 F.3d 1354, 1367 (Fed. Cir. 2004)). Hodge merely discloses preparation of antibodies against IL-21R using conventional monoclonal antibody technology. (See, Example 4). Although Hodge does make antibodies using the same polypeptide as was used to make 18A5, the antibodies of Hodge and 18A5 do not necessarily bind the same epitope on the receptor, such that they compete for each other's binding. A typical antibody epitope comprises 8-10 amino acids of an antigen. Thus, in order for the antibodies of Hodge to compete with the claimed antibodies, e.g., 18A5, the antibodies of Hodge must bind to at least some of the same 8-10 amino acids of the 235 amino acid long extracellular domain of IL-21R bound by Applicants' antibodies.

The antibodies of Hodge and Applicants' antibodies were made using distinct methods. The antibodies of Hodge were made by injecting mice with an IL-21R-IgG fusion protein, followed by standard monoclonal antibody selection technology. (See, Hodge,

Example 4). The antibody of the present invention was made by scFv phagemid library selection on an IL-21R-expressing cell line. (See, Example 3). Because different methodologies were used to prepare the Hodge antibodies and Applicants' antibodies, it is likely that different epitopes of the IL-21R antigen were available for antibody selection. It is important to note, however, that even if the same antibody production methodology was used, the Hodge antibodies and Applicants' antibodies would not necessarily recognize the same antigen. For instance, the instant specification teaches that the 18A5 and 18G4 antibodies were both produced by scFv phage library selection on IL-21R-expressing cells. (*Specification*, Example 3). Yet, the specification also teaches that the 18A5 and 18G4 antibodies may bind to distinct epitopes on IL-21R. (*Id.*, Example 11; teaching that 18G4 strongly competes with MUF antibody in an epitope competition assay, while 18A5 is a much weaker competitor). Therefore, one of ordinary skill in the art would recognize that the antibodies disclosed in Hodge do not necessarily compete with Applicants' antibodies for binding to IL-21R. Thus, Applicants respectfully submit that the antibodies of the present invention are not inherently disclosed in Hodge, and respectfully request withdrawal of this inherency-based rejection of claims 6-13, 15 and 38.

Regarding claim 39, the claim essentially teaches an antibody made by inserting a CDR of SEQ ID NOs:68, 69, 70, 71, 72 or 73 into an existing antibody or an antigen-binding fragment. Thus, an antibody of claim 39 would contain at least one CDR selected from the above sequences. Because Hodge does not teach any antibodies containing these specific sequences, and Hodge does not suggest or provide any motivation to make antibodies containing

these specific sequences, Hodge does not inherently anticipate or render obvious the antibodies recited in claim 39 (or new claim 40).

For at least these reasons, Applicants respectfully request the withdrawal of the anticipation-based and obviousness-based rejections of claims 6-13, 15, 38 and 39.

CONCLUSION

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns have been answered and overcome, that the presently claimed invention satisfies 35 U.S.C. §112, and that the instant claims are neither disclosed nor suggested by any art of record. Accordingly, reconsideration and allowance of all claims are earnestly solicited.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below-listed address.

Respectfully submitted,

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